

Council of State and Territorial Epidemiologists
Position Statement

04-ID-01

Committee: **Infectious Disease**

Title: **Revision of the National Surveillance Case Definition of Diseases Caused by Neurotropic Domestic Arboviruses, Including the Addition to the NNDSS of Non-Neuroinvasive Illnesses Caused by these Viruses**

Statement of the problem:

Arthropod-borne viruses (arboviruses) are transmitted to people primarily by the bite of infected arthropods, typically mosquitoes or ticks. Neurotropic arboviruses can cause asymptomatic infections or clinical illnesses that range in severity from self-limited non-localized febrile illnesses to severe and sometimes fatal neurologic syndromes, including meningitis, myelitis, encephalitis, neuritis and other neuropathies, such as Guillain-Barré syndrome. Rarely, neurotropic arboviruses have also been reported to cause visceral diseases such as pancreatitis, myocarditis, and hepatitis.

Currently, encephalitis and meningitis caused by infection with six neurotropic arboviruses (St. Louis encephalitis, West Nile, Powassan, eastern equine encephalitis, western equine encephalitis, and the California serogroup viruses) are nationally reportable. Since 1999, with the introduction and spread of West Nile virus (WNV) in the United States, the numbers of reported cases of neuroinvasive WNV disease have grown tremendously. Most WNV infections are asymptomatic, and probably less than 5% of symptomatic cases are encephalitis or meningitis. The majority of symptomatic WNV disease cases are mild, usually with self-limited fever, headache, arthralgias, myalgias, and/or fatigue, and these are not currently included in the case definition for arboviral encephalitis or meningitis, or in the NNDSS. The Centers for Disease Control and Prevention (CDC) has recommended that jurisdictions voluntarily report West Nile fever (WNF) cases so that there is more comprehensive tracking of WNV activity and monitoring of symptomatic infections. In 2002, CDC recommended a surveillance case definition for WNF, which has never been adopted by the Council of State and Territorial Epidemiologists (CSTE). In addition, since 1999, acute WNV myelitis ("WNV poliomyelitis") cases with paralysis, as well as WNV neuritis/neuropathy cases, have been increasingly recognized in North America, and many of these cases are not associated with encephalitis or meningitis and are therefore not consistently reported to the NNDSS.

Because of a lack of national adoption of a broader case definition of WNV disease, or a consensus regarding adding WNV myelitis, WNV neuritis/neuropathy, and WNF and other non-neuroinvasive WNV-associated illnesses to the NNDSS, there is non-uniform reporting of WNV disease among jurisdictions. This situation has resulted in incomplete and, more importantly, non-uniform tracking of the WNV epidemic across jurisdictions.

Statement of the desired action(s) to be taken:

1. Expand the current national surveillance case definition of neuroinvasive arboviral encephalitis and meningitis due to West Nile, St. Louis encephalitis, Powassan, eastern equine encephalitis, western equine encephalitis, and California serogroup viruses to include neurological syndromes other than encephalitis and meningitis (e.g., WNV myelitis and neuritis/neuropathy), as well as non-neuroinvasive illnesses caused by these viruses (e.g., WNF). (See proposed case definition attached).
2. Add neurological syndromes other than encephalitis and meningitis (e.g., myelitis and neuritis/neuropathy), as well as non-neuroinvasive illnesses caused by these viruses, to the NNDSS.

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Goals of Surveillance:

- 1) Assess the national public health impact of both neuroinvasive and non-neuroinvasive disease caused by WNV and selected other neurotropic arboviruses and monitor national trends.
- 2) Demonstrate the need for public health intervention programs and federal resources, and provide data to allocate resources.
- 3) Identify high-risk population groups or geographic areas to target interventions and guide analytic studies.
- 4) Develop hypotheses leading to analytic studies about risk factors for infection and disease.

Methods of Surveillance:

Both probable and confirmed cases are reported to the NNDSS.

Case Definition: See attached.

Period of Surveillance: Indefinite

Background and Justification:

Historically, national surveillance for arboviral diseases has focused on encephalitis and meningitis cases due to infection with St. Louis encephalitis, eastern equine encephalitis, western equine encephalitis, and California serogroup viruses (especially La Crosse virus). Prior to the introduction of WNV into the United States, most domestic arboviral disease cases reported to CDC were cases of encephalitis or meningitis; few, if any, cases of myelitis or neuritis/neuropathy were reported. Incorporating selected non-neuroinvasive illnesses due to infections with domestic arboviruses other than WNV is not expected to greatly increase the number of reported cases of disease because of the relatively low incidence of infections with St. Louis encephalitis, Powassan, eastern equine encephalitis, western equine encephalitis, and California serogroup viruses, the five other arboviruses currently included in the NNDSS. The addition of WNF to the NNDSS, however, could greatly increase the total number of nationally reportable WNV disease cases. For example, approximately 3,000 neuroinvasive WNV disease cases were reported to CDC in 2003; surveillance for these types of cases is considered to be reasonably complete. It is crudely estimated that about 20 WNF cases occur for every neuroinvasive WNV disease case. Therefore, it is estimated that as many as 60,000 WNF cases may have occurred nationally in 2003. However, surveillance for WNF is incomplete. In 2003, approximately 7,500 WNF cases were reported to CDC. This small number of reported cases is probably due to the small proportion of WNF cases that come to medical attention, the fewer yet that are tested serologically, and the fewer yet that are reported to state health departments. Although adding WNF to the NNDSS would increase the burden of reporting for some jurisdictions, some states have already changed their reporting regulations to include WNF, and many are already reporting WNF cases to CDC via ArboNET. CSTE's adoption of a broader national surveillance case definition that includes neurological syndromes other than encephalitis and meningitis (e.g., WNV myelitis and neuritis/neuropathy) and non-neuroinvasive illnesses due to infection with neurotropic domestic arboviruses will bring the current CSTE-approved case definition into alignment with current surveillance practice. Also, adding these conditions to the NNDSS will encourage more uniform national surveillance and promote more comparable data collection across jurisdictions.

Coordination:

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CASE DEFINITION: Neurotropic Domestic Arboviral Diseases

Clinical description

Arboviral infections may be asymptomatic or may result in febrile illnesses of variable severity sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes include aseptic meningitis, myelitis and encephalitis, which are clinically indistinguishable from similar syndromes caused by other viruses. Arboviral meningitis is usually characterized by fever, headache, stiff neck, and pleocytosis in cerebrospinal fluid. Arboviral myelitis is usually characterized by fever and acute limb paresis or flaccid paralysis. Arboviral encephalitis is usually characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction. Less common neurological syndromes can include cranial and peripheral neuritis/neuropathies, including Guillain-Barré syndrome.

Non-neuroinvasive syndromes caused by these usually neurotropic arboviruses can rarely include myocarditis, pancreatitis, or hepatitis. In addition, they may cause febrile illnesses (e.g., West Nile fever [WNF]) that are non-localized, self-limited illnesses with headache, myalgias, arthralgias, and sometimes accompanied by skin rash or lymphadenopathy. Laboratory-confirmed arboviral illnesses lacking documented fever can occur, and overlap among the various clinical syndromes is common.

Clinical criteria for diagnosis

Cases of arboviral disease are classified either as neuroinvasive or non-neuroinvasive, according to the following criteria:

Neuroinvasive disease requires the presence of fever and at least one of the following, as documented by a physician and in the absence of a more likely clinical explanation:

- Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma), or
- Other acute signs of central or peripheral neurologic dysfunction (e.g., paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements), or
- Pleocytosis (increased white blood cell concentration in cerebrospinal fluid [CSF]) associated with illness clinically compatible with meningitis (e.g., headache or stiff neck).

Non-neuroinvasive disease requires, at minimum, the presence of documented fever, as measured by the patient or clinician, the absence of neuroinvasive disease (above), and the absence of a more likely clinical explanation for the illness. Involvement of non-neurological organs (e.g., heart, pancreas, liver) should be documented using standard clinico-laboratory criteria.

Laboratory criteria for diagnosis

Cases of arboviral disease are also classified either as confirmed or probable, according to the following laboratory criteria:

Confirmed case:

- Fourfold or greater change in virus-specific serum antibody titer, or

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- Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, CSF, or other body fluid, or
- Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
- Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Probable case:

- Stable (less than or equal to a twofold change) but elevated titer of virus-specific serum antibodies, or
- Virus-specific serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.

Case definition

A case must meet one or more of the above clinical criteria and one or more of the above laboratory criteria.

Comment

Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic tests using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in areas where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization tests using an appropriate battery of closely related viruses. This is essential, for example, in determining that antibodies detected against St. Louis encephalitis virus are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur. Because dengue fever and West Nile fever can be clinically indistinguishable, the importance of a recent travel history and appropriate serologic testing cannot be overemphasized. In some persons, West Nile virus-specific serum IgM antibody can wane slowly and be detectable for more than one year following infection. Therefore, in areas where West Nile virus has circulated in the recent past, the co-existence of West Nile virus-specific IgM antibody and illness in a given case may be coincidental and unrelated. In those areas, the testing of serially collected serum specimens assumes added importance.

The seasonality of arboviral transmission is variable and depends on the geographic location of exposure, the specific cycles of viral transmission, and local climatic conditions. Reporting should be etiology-specific (see below; the six diseases printed in bold are nationally reportable to CDC):

- **St. Louis encephalitis virus disease**
- **West Nile virus disease**
- **Powassan virus disease**
- **Eastern equine encephalitis virus disease**

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- **Western equine virus disease**
- **California serogroup virus disease** (includes infections with the following viruses: La Crosse, Jamestown Canyon, snowshoe hare, trivittatus, Keystone, and California encephalitis viruses)

Note: Due to the continued risk of unintentional or intentional introduction of exotic arboviruses into the United States (e.g., Venezuelan equine encephalitis virus), or the reemergence of indigenous epidemic arboviruses (e.g., St. Louis encephalitis and western equine encephalitis viruses), physicians and local public health officials should maintain a high index of clinical suspicion for cases of potential exotic or unusual arboviral etiology, and consider early consultation with arboviral disease experts at state health departments and CDC.